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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/934,680	MCBRANCH ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *14-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *8/23/2001 (original)* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7/2004* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on July 22, 2004 has been entered. The claims pending in this application are claims 1-24 with claims 14-21 withdrawn from consideration as the result of the restriction requirement. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on July 22, 2004.

Claim Objections

2. Claims 1 and 6 are objected to because of the following informality: "a plurality of fluorescers attached to or part of a conjugated backbone" should be "a plurality of fluorescers attached to a conjugated backbone or part of a conjugated backbone".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To the extent that the claimed composition/or methods are not described in the instant disclosure, claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

The recitation " the fluorescer molecules comprise a plurality of fluorescers pendent on a non-conjugated polymer backbone" is added to the new claim 23. Although the specification describes that dye polymers that have an ionic fluorescent dye chromophore on each repeat unit on a non-conjugated polymer have previously been shown to exhibit strong J-aggregate absorption and fluorescence (e.g., see page 10, second paragraph), the specification fails to define or provide any disclosure to support such claim recitation. Furthermore, in applicant's remarks filed on January 20, 2004, applicant does not indicate which part in the specification supports such claim recitation.

MPEP 2163.06 notes "IF NEW MATTER IS ADDED TO THE CLAIMS, THE EXAMINER SHOULD REJECT THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH - WRITTEN DESCRIPTION REQUIREMENT. *IN RE RASMUSSEN*, 650 F.2D 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application." MPEP 2163.06 further notes "WHEN AN AMENDMENT IS FILED IN REPLY TO AN OBJECTION OR REJECTION BASED ON 35 U.S.C. 112, FIRST PARAGRAPH, A STUDY OF THE ENTIRE APPLICATION IS OFTEN NECESSARY TO DETERMINE

WHETHER OR NOT "NEW MATTER" IS INVOLVED. *APPLICANT SHOULD THEREFORE SPECIFICALLY POINT OUT THE SUPPORT FOR ANY AMENDMENTS MADE TO THE DISCLOSURE*" (emphasis added).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 4-8, 12, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Heller (US Patent No. 5,849,489, published on December 15, 1998).

Heller teaches hybridization of polynucleotides conjugated with chromophores and fluorophores to generate donor-to-donor energy transfer system.

Regarding claim 1, as shown in Figures 2A, Heller teaches a complex formed by a single DNA polynucleotide strand with multiple donors groups (D) and a single acceptor group (A) and a template DNA oligomer (e.g., see Figure 2A and column 6, lines 20-23). Since the single DNA polynucleotide strand taught by Heller includes a 5' portion having multiple fluorescence donors (e.g., see attached Figure 2A with the examiner's handwritings in this office action and column 11, lines 23-39), Heller discloses a fluorescent moiety comprising a plurality of fluorescers (ie., 5' portion of the single DNA polynucleotide strand having multiple fluorescence donors) recited in the claim. Since the fluorescent polymer in the single DNA polynucleotide strand taught by Heller connects with a first tethering element which connects with a recognition element and a target nucleic acid (ie., template DNA) (see attached Figure 2A with the examiner's handwritings in this office action), Heller discloses a recognition element which

binds to a target nucleic acid wherein the recognition element is bonded to the fluorescent polymer by a first tethering element as recited in the claim. Since the single DNA polynucleotide strand taught by Heller includes a 3' portion having a fluorescence acceptor that connects with a second tethering element (e.g., see attached Figure 2A with the examiner's handwritings in this office action and column 11, lines 25-39), the 3' portion having a fluorescence acceptor in the single DNA polynucleotide strand taught by Heller is a property altering element and Heller discloses a property altering element bonded to the recognition element by a second tethering element as recited in the claim. Since the single DNA polynucleotide strand taught by Heller attaches multiple donors and an acceptor (e.g., see attached Figure 2A with the examiner's handwritings in this office action) and the bases of the single DNA polynucleotide strand taught by Heller are connected by 3', 5'-phosphodiester bonds, Heller teaches a plurality of fluorescers attached to a conjugated backbone (ie., the single DNA polynucleotide strand) as recited in the claim. Since Heller teaches that the single DNA polynucleotide strand attached multiple donors and an acceptor is used to hybridize with a target nucleic acid and the presence of photonic energy emitted from the excited acceptor chromophore is used to detect the presence of the target nucleic acid (see column 18, lines 32-67 and column 19, lines 1-46), the fluorescence emitted by the fluorescent moiety must be different from that emitted when the recognition element does not bind to the single DNA polynucleotide strand attached multiple donors and an acceptor to the target nucleic acid. Thus Heller discloses that, in the presence of binding of the recognition element to a target nucleic acid, the fluorescence emitted by the fluorescent moiety is altered from that emitted when binding between the recognition element and the target nucleic acid does not occur as recited in the claim.

Regarding claim 4, since Heller teaches that the property altering element is the 3' portion having a fluorescence acceptor in the single DNA polynucleotide strand (see attached Figure 2A with the examiner's handwritings in this office action), Heller discloses that said property altering element is selected from the group consisting of methyl viologen, quinones, metal complexes, fluorescent dyes, nonfluorescent dyes and energy accepting, electron accepting and electron donating moiety as recited in claim 4.

Regarding claim 5, as shown in the rejection on claim 1, since the fluorescence polymer (ie., the 5' portion having a fluorescence acceptor in the single DNA polynucleotide strand taught by Heller in Figure 2A) connects with the recognition element by the first tethering element while the property altering element (ie., a 3' portion having multiple fluorescence donors in the single DNA polynucleotide strand taught by Heller in Figure 2A) connects with the recognition element by the second tethering element (see attached Figure 2A with the examiner's handwritings in this office action), the first tethering element or second tethering element can be a single phosphodiester bond that is used to connect two adjacent nucleotides of the single DNA polynucleotide strand taught by Heller in Figure 2A. Therefore, Heller discloses that said first and second tethering elements are selected from the group consisting of a single bond (ie., a single phosphodiester bond), a single divalent atom, a divalent chemical moiety of up to 10 carbon atoms in length and a multivalent chemical moiety as recited in claim 5.

Regarding claims 6-8, since Heller teaches that at least two identical donors chromophores are attached to 5' portion of the single DNA polynucleotide by linker arms (e.g., see attached Figure 2A with the examiner's handwritings in this office action, lines 59-65 of column 4, and ID2 in top of column 23) wherein the linker arms are linker arm nucleosides such

as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite (e.g., see column 14, lines 55-67), Heller discloses that said fluorescent moiety (ie., the 5' portion having a fluorescence acceptor in the single DNA polynucleotide strand taught by Heller in Figure 2A) comprises a plurality of fluorescers attached to a conjugated backbone (ie., the single DNA polynucleotide strand) as recited in claim 6. Since Heller teaches that at least two identical donors chromophores are attached to 5' portion of the single DNA polynucleotide by linker arms (see attached Figure 2A with the examiner's handwritings in this office action), Heller discloses that said fluorescent moiety (ie., 5' portion having multiple fluorescence donors in the single DNA polynucleotide in Figure 2A) comprises repeat units (ie., donor chromophores plus linker arm nucleosides such as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite) each containing a fluorescent dye pendant on a backbone moiety (ie., a base in 5' portion of the single DNA polynucleotide in Figure 2A) as recited in claim 8. Since the fluorescent polymer (ie., 5' portion having multiple fluorescence donors in the single DNA polynucleotide in Figure 2A) comprises a nucleic acid, which carries negative charges and comprising a plurality of conjugated bases, Heller discloses that said fluorescent polymer is an anionic conjugated polymer as recited in claim 7.

Regarding claims 12 and 13, since Heller teaches that a single DNA polynucleotide strand with multiple donors groups (D) and a single acceptor group (A) is covalently or noncovalently linked to a solid support such as an organic polymer (see column 8, first paragraph), Heller discloses that said fluorescent moiety (ie., a 5' portion having multiple fluorescence donors in the single DNA polynucleotide strand taught by Heller in Figure 2A) is affixed to a support as recited in claim 12 wherein said support is selected from the group

consisting of a fiber optic, a flexible plastic substrate, porous beads, solid beads, organic polymers, natural clays, synthetic clays particles, membranes, microporous gels and silica as recited in claim 13.

Therefore, Heller teaches all limitations recited in claims 1, 4-8, 12, and 13.

Response to Arguments

In page 7, last paragraph bridging to page 8, first paragraph of applicant's remarks, applicant argues that "[A]ccording to the Official Action, Heller discloses a complex formed by a single DNA polynucleotide strand with multiple donor groups (D) and a single acceptor group (A) (FIG. 2A of Heller, pg. 4 of the Office Action). This complex, however, is not a 'fluorescent moiety' as defined in amended Claim 1. In particular, according to Claim 1, the 'fluorescent moiety' comprises a plurality of fluorescers attached to or part of a conjugated polymer backbone or a J-aggregate of a plurality of fluorescer molecules. Conjugated polymers comprise a chain or backbone of alternating double and single bonds. The polynucleotides disclosed in Heller clearly do not comprise a conjugated backbone. Further, there is no teaching or suggestion in Heller of J-aggregates. The term 'J-aggregate' refers to aggregates of fluorescer molecules (i.e., monomers) that exhibit an absorption band different from the individual monomers making up the aggregate. In the case of J-aggregates, the absorption band is shifted to higher wavelengths (See, for example, Daehne et al., 'surface Morphological Studies of J-Agregate Thin Films by Atomic Force Microscopy', Langmuir, pp. 565-568 (1998)). Accordingly, it is respectfully submitted that Heller does not teach or reasonably suggest the invention as defined by Claim 1".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, in the office action, the examiner has clearly indicated that 5' portion of the single DNA polynucleotide strand having multiple fluorescence donors is a fluorescent moiety wherein a plurality of fluorescers attached to a conjugated backbone (ie., the single DNA polynucleotide strand) as recited in claim 1 (see above rejection under 35 U. S. C 102). Second, there is no definition for "J-aggregate" in the specification. Third, claim 1 does not require that conjugated polymers comprise a chain or backbone of alternating double and single bonds and J-aggregates are aggregates of fluorescer molecules (i.e., monomers) that exhibit an absorption band different from the individual monomers making up the aggregate wherein the absorption band is shifted to higher wavelengths as suggested by applicant. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

7. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Heller (December 15, 1998) as applied to claims 1, 4-8, 12, and 13 above as evidence by Woódrum (US Patent No. 4,959,305, published on September 25, 1990).

The teachings of Heller have been summarized previously, *supra*.

Regarding claim 11, since Heller teaches that donors chromophores attached to 5' portion of the single DNA polynucleotide in Figure 2A (see Figure 2A) can be fluorescein (see column 11, lines 23-39) and it is known that fluorescein carries a negative charge (see Woodrum, column

11, lines 41-46), Heller as evidence by Woodrum discloses that said fluorescent dye is a negative charged dye chromophore as recited in claim 11.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (December 15, 1998) as applied to claims 1, 4-8, 12, and 13 above, and further in view of Coull *et al.*, (US Patent No. 6,355,421 B1, filed on October 27, 1998).

The teachings of Heller have been summarized previously, *supra.*

Heller does not disclose that said recognition element is a sequence of peptide nucleic acids that can recognize and hybridize with said target nucleic acid as recited in claim 2 wherein said sequence of peptide nucleic acids is a base sequence complementary to a member selected

from the group consisting of a sequence of single stranded DNA and a sequence of single stranded RNA as recited in claim 3.

Coull *et al.*, teach methods, kits, and compositions pertaining to PNA molecular beacons.

Regarding claims 2 and 3, Coull *et al.*, teach that peptide nucleic acid (PNA) hybridizes to DNA or RNA with sequence specificity (see column 5, lines 31-46) and stability of the PNA/nucleic acid complex is higher than that of an analogous DNA/DNA or RNA/DNA complex (see column 6, last paragraph). Therefore, Coull *et al.*, disclose a sequence of peptide nucleic acids is a base sequence complementary to a member selected from the group consisting of a sequence of single stranded DNA and a sequence of single stranded RNA as recited in claim 3.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a chemical moiety comprising a recognition element as recited in claims 2 and 3 wherein said recognition element is a sequence of peptide nucleic acids that can recognize and hybridize with said target nucleic acid in view of the patents of Heller and Coull *et al.*. One having ordinary skill in the art would have been motivated to do so because incorporation of PNA into the recognition element of the chemical moiety recited in claim 1 to form the chemical moiety recited in claims 2 and 3 would enhance stability of the chemical moiety recited in claim 1 and increase half-life of the chemical moiety recited in claim 1 (see Coull *et al.*, column 5, last paragraph) since PNA is not sensitive to nuclease digestion (see Coull *et al.*, column 4, second paragraph), and would enhance to form a more stable complex between the recognition element of the chemical moiety recited in claim 1 and a target nucleic acid (see Coull *et al.*, column 6, last paragraph). One having ordinary skill in the art at

the time the invention was made would have been a reasonable expectation of success to make a chemical moiety comprising a recognition element comprising a PNA as recited in claims 2 and 3.

10. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (December 15, 1998) as applied to claims 1, 4-8, 12, and 13 above.

The teachings of Heller have been summarized previously, *supra*. Although Heller does not teach that the number of repeat units is greater than or equal to 33 as recited in claim 9, Heller disclose that the fluorescent polymer (ie., 5' portion having multiple fluorescence donors in the single DNA polynucleotide in Figure 2A) comprises at least two repeat units (ie., donor chromophores plus linker arm nucleosides such as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite) (see column 4, lines 59-67, and column 14, lines 55-67) and about 10 donors are incorporated in a single oligonucleotide sequence of 50 nucleotides (see column 13, lines 45-67) (ie., 10 donor chromophores plus 10 linker arm nucleosides).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a nucleic acid with a fluorescent polymer comprising repeat units (ie., donor chromophores plus linker arm nucleosides such as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite) as recited in claim 9 wherein the number of repeat units is greater than or equal to 33 in view of Heller's patent. One having ordinary skill in the art has been motivated to do so because optimization of the number of repeat units (ie., donors chromophores plus linker arm nucleosides

such as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite) in the fluorescent polymer (ie., 5' portion having multiple fluorescence donors in the single DNA polynucleotide in Figure 2A) of the chemical moiety recited in claim 8 would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to optimize the number of repeat units (ie., donors chromophores plus linker arm nucleosides such as 5'-dimethoxytrityl-5[N-(7-trifluoroacetylaminoheptyl)-2'-deoxyuridine 3'-O-phosphoramidite) in the fluorescent polymer (ie., 3' portion having multiple fluorescence donors in the single DNA polynucleotide in Figure 2A) of the chemical moiety recited in claim 8 during the process of making the chemical moiety recited in claim 9. Note that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

11. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (December 15, 1998) as applied to claims 1, 4-9, 12, and 13 above, and further in view of Chen *et al.*, (PNAS, 96, 12287-12292, October 1999).

The teachings of Heller have been summarized previously, *supra.*

Heller does not disclose that said fluorescent moiety is a J-aggregate of a plurality of fluorescer molecules as recited in claim 10.

Chen *et al.*, teach highly sensitive biological and chemical sensors based on reversible fluorescence quenching in a conjugated polymer. One of fluorescent polyanionic conjugated polymers, poly (MPS-PPV), comprising about 1000 identical monomer repeat units with fluorescences and the use of this fluorescence polymer leads to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see page 12287).

Regarding claim 10, although the specification describes that J-aggregate, there is no definition for "J-aggregate" in the specification. Since MPS-PPV becomes an aggregate in the presence of divalent cations (see page 12289, right column), which is a J shape (see Figure 2A, right drawing), in a broad and reasonable interpretation, MPS-PPV is a fluorescent monomer that can form a J-aggregate of a plurality of fluorescer molecules (ie., MPS-PPV) as recited in claim 10.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a chemical moiety comprising a fluorescent moiety wherein said fluorescent moiety is a J-aggregate of a plurality of fluorescer molecules (ie., MPS-PPV) as recited in claim 10 in view of the prior art of Heller and Chen *et al.*. One having ordinary skill in the art would have been motivated to do so because the use of the fluorescence moiety taught by Chen *et al.*, would lead to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see Chen *et al.*, page 12287). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a chemical moiety comprising a fluorescent moiety wherein said fluorescent moiety is a J-

aggregate of a plurality of fluorescer molecules (ie., MPS-PPV) as recited in claim 10 since Chen *et al.,* have successfully made or used a fluorescent moiety as recited in claim 10.

Response to Arguments

In page 8, second paragraph bridging to page 9, first paragraph of applicant's remarks, applicant argues that "[I]t is respectfully submitted that the other references cited in the Official Action do not remedy the above noted deficiencies of Heller. First, the Official Action has pointed to no teaching or suggestion in any of Woodrum or Coull which would reasonably suggest the chemical moiety as set forth in Claim 1. In fact, Coull is merely being relied upon for its teaching of peptide nucleic acids (pg. 9 of the Official Action) and Woodrum is merely being relied upon as evidence that fluorescein carries a negative charge (pg. 8 of the Official Action). Further, while Chen discloses assays employing a fluorescent conjugated polymer (i.e., MPS-PPV), the proposed combination of Heller and Chen would render the complex disclosed by Heller unfit for its intended purpose. In particular, Heller relies upon the hybridization of the polynucleotide strand to which the donor chromophores are attached to achieve the appropriate spacing for efficient donor-donor and donor-acceptor energy transfer (FIG. 2A of Heller). The fluorescent polymer of Chen does not have a polynucleotide backbone and would therefore not hybridize to a target nucleic acid. Accordingly, substitution of the MPS-PPV polymer of Chen in the complex of Heller would result in a complex which is unfit for its intended purpose (i.e., hybridization to a target resulting in efficient donor-donor and donor-acceptor energy transfer). Heller also teaches away from the proposed combination. In particular, Heller relies upon the spacing of the donor-donor pairs at specified distances on the polynucleotide strand (Column 13, Lines 45-59 of Heller). In fact, Heller teaches that close spacing of the donor-donor pairs can

reduce energy transfer efficiency. As set forth in the attached declaration, the chromophore in fluorescent polymers such as MPS-PPV have much closer spacings than those disclosed in Heller".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the patent of Woodrum is only used to provide an evidence that fluorescein carries a negative charge since Heller teaches to use fluorescein as a donor while Coull *et al.*, provide a motivation to incorporate PNA into the recognition element of the chemical moiety (see above rejection on claims 2, 3, and 11). Second, although "the fluorescent polymer of Chen does not have a polynucleotide backbone and would therefore not hybridize to a target nucleic acid", the rejection on claim 10 is not based on that fluorescent polymer of Chen *et al.*, have a polynucleotide backbone and would therefore not hybridize to a target nucleic acid. The rejection is based on a motivation because the use of the fluorescence moiety taught by Chen *et al.*, would lead to a greater than million-fold amplification of the sensitivity to fluorescence quenching relative to that of corresponding small conjugated molecules with similar structure (see above rejection on claim 10). Thus, substitution of the MPS-PPV polymer of Chen *et al.*, in the complex of Heller would result in a complex which is unfit for its intended purpose as suggested by applicant is incorrect. Third, although applicant declaration filed on July 22, 2004 states that the chromophore in fluorescent polymers such as MPS-PPV have much closer spacings than those disclosed in Heller, the spacing among these MPS-PPV is not related to spacings among donors taught by Heller because, in the rejection on claim 10, the donors taught by Heller are replaced by of MPS-PPV polymer and is not substituted by MPS-PPV monomer.

12. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (December 15, 1998) as applied to claims 1, 4-9, 12, and 13 above, and further in view of Chick et al., (US Patent No. 5,342,789, published on August 30, 1994).

The teachings of Heller have been summarized previously, *supra.*

Heller does not disclose that the property altering element is non-fluorescent as recited in claim 22.

it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have used a transition metal complex comprising an iron atom as an electron transfer moiety as recited in claims 26 and 32 in view of the patent of Bannwarth *et al.*. One having ordinary skill in the art would have been motivated to do so because both ruthenium and iron are belong to transition metal VIIIB and the simple replacement of one chemical element (ie., ruthenium) from another chemical element with a similar properties during the process of making a transition metal complex would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the intended use of the transition metal complex.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.06, 2144.07, and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-13 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 10/098,387. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 1-13 in this instant application are not identical to claims 1-14 of copending Application No. 10/098,387, claims 1-14 in copending Application No. 10/098,387 are directed to the same subject matter and fall entirely within the scope of claims 1-13 in this instant application. In other words, claims 1-13 in this instant application are anticipated by claims 1-14 of copending Application No. 10/098,387.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

In page 6, fourth and fifth paragraphs of applicant's remarks, applicant argues that "[A]ttached hereto is a Terminal Disclaimer over U.S. Patent Application Serial No. 10/098,387. It is respectfully submitted that the filing of this terminal disclaimer obviates this rejection. Reconsideration and withdrawal of this rejection is therefore respectfully requested".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because the examiner cannot locate a terminal disclaimer.

14. The declaration under 37 CFR 1.132 filed on July 22, 2004 is insufficient to overcome the rejection of claim 10 based upon that "[T]he MPS-PPV polymers in Chen comprise chromophores with much closer spacings than 4 or 5 oligonucleotide spacings disclosed in Heller as set forth in the last Office action because the spacing among these MPS-PPV is not related to spacings among donors taught by Heller since, in the rejection on claim 10, the donors

taught by Heller are replaced by of MPS-PPV polymer and is not substituted by MPS-PPV monomer.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. No claim is allowed.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)272-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
November 16, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
11/17/04